

Table S1. Bacterial strains and primers used in this work.

| Number | Description/Sequence | Source/Reference |
|---------------|--|------------------|
| Strain number | Strain description/genotype | Source |
| YP03.5 | <i>Yersinia pestis</i> CO92, wild-type (<i>pCD1</i> ⁺ , <i>pMT1</i> ⁺ , <i>pPCP1</i> ⁺ , <i>pgm</i> ⁺) | 1 |
| YP489 | <i>Y. pestis</i> CO92 Δyop [<i>ΔyopE</i> ΔKO1 (<i>yopH</i> , <i>ypkA</i> , <i>yopJ</i>), ΔKO2 (<i>yopT</i> , <i>yopM</i> , <i>yopQ</i>)] | This study |
| YP266-1 | <i>Y. pestis</i> CO92 Δ <i>yopE</i> | 2 |
| YP373-1 | <i>Y. pestis</i> CO92 Δ <i>yopH</i> | 3 |
| YP100 | <i>Y. pestis</i> CO92 Δ <i>yopJ</i> | 2 |
| YP268-1 | <i>Y. pestis</i> CO92 Δ <i>yopT</i> | 2 |
| YP267-1 | <i>Y. pestis</i> CO92 Δ <i>yopM</i> | 2 |
| YP269-1 | <i>Y. pestis</i> CO92 Δ <i>ypkA</i> | 2 |
| YP487-1 | <i>Y. pestis</i> CO92 Δ <i>yopE/yopH/yopJ/ypkA</i> | This study |
| YP528 | <i>Y. pestis</i> CO92 Δ <i>yopT/yopM/yopQ</i> | This study |
| YP493 | <i>Y. pestis</i> CO92 Δ <i>yopE/yopH</i> | This study |
| YP529 | <i>Y. pestis</i> CO92 Δ <i>yopE/yopJ</i> | This study |
| YP500-2 | <i>Y. pestis</i> CO92 Δ <i>yopE/ypkA</i> | This study |
| YP526 | <i>Y. pestis</i> CO92 Δ <i>yopH/yopJ</i> | This study |
| YP525 | <i>Y. pestis</i> CO92 Δ <i>yopH/ypkA</i> | This study |
| YP522 | <i>Y. pestis</i> CO92 Δ <i>ypkA/yopJ</i> | This study |
| YP520 | <i>Y. pestis</i> CO92 <i>yopE</i> only [ΔKO1 (<i>yopH</i> , <i>ypkA</i> , <i>yopJ</i>) ΔKO2 (<i>yopT</i> , <i>yopM</i> , <i>yopQ</i>)] | This study |
| YP517-1 | <i>Y. pestis</i> CO92 <i>yopH</i> only [Δ <i>yopE</i> ΔKO2 (<i>yopT</i> , <i>yopM</i> , <i>yopQ</i>) <i>ypkA-yopJ::kan</i>] | This study |
| YP533-2 | <i>Y. pestis</i> CO92 <i>yopEH</i> only [ΔKO2 (<i>yopT</i> , <i>yopM</i> , <i>yopQ</i>) Δ <i>ypkA-yopJ</i>] | This study |
| YPI134-1 | <i>Y. pestis</i> CO92 YopE-TEM | 4 |
| VK148 | <i>Klebsiella pneumoniae</i> KPPR1S, <i>Rif</i> ^R and <i>Str</i> ^R derivative of ATCC 43816 | 5 |
| KE52 | <i>Escherichia coli</i> S17 pSR47S-KO1 | This study |
| Primer number | Primer name and Sequence | Source |
| BG2930 | <i>yopE</i> up F, 5'-TAGTGAGTTATTATCCAGGCTGTT-3' | This study |
| BG2931 | <i>yopE</i> up R + P1, 5'-GAAGCAGCTCCAGCCTACACCATGACTATTATTACCTTGGCTATTA-3' | This study |
| BG2932 | <i>yopE</i> down F + P4, 5'-GGTCGACGGATCCCCGGAATTGATATGGATAAAAACAAGGGGATAG-3' | This study |
| BG2933 | <i>yopE</i> down R, 5'-ATGTACCTGTGAGCCATCGTTAAC-3' | This study |
| BG2971 | KO1 upstream F, 5'- GTCGACAATATGCCACCCGTTATCTATG-3' | This study |
| BG2972 | KO1 upstream R, 5'-GGATCCCACCACTTGCCAATCAAAGAAC-3' | This study |
| BG2973 | KO1 downstream F, 5'-GGATCCCATGCTTACTCATCCCCAT-3' | This study |
| BG2974 | KO1 downstream R, 5'-GC GGCC CGC ATT CTGGGACGGGTTAAC-3' | This study |
| BG2977 | KO2 upstream F, 5'-GTCGACAACAGGGCATGGCACCTCCC-3' | This study |
| BG2989 | KO2 upstream R + P1, 5'-GAAGCAGCTCCAGCCTACACGGATGAAGCTATATTAAAGAG-3' | This study |
| BG2990 | KO2 downstream F + P4, 5'-GGTCGACGGATCCCCGGAATCATATTGAATGCCTTCTG-3' | This study |
| BG2978 | KO2 downstream R, 5'-GC GGCC CGCC CTTGACGGTTCAAAA-3' | This study |
| BG3006 | KO1 site R, 5'-GCCCATAGACTCCTCTATGCTTAAG-3' | This study |
| BG3011 | <i>yopH</i> up F, 5'-TCGCACGGAAA ACTGCATCC-3' | This study |
| BG3012 | <i>yopH</i> up R + P1, 5'-GAAGCAGCTCCAGCCTACACCATGCTCCCTCCTTAATTAA-3' | This study |
| BG3013 | <i>yopH</i> down F + P4, 5'-GGTCGACGGATCCCCGGAATTAAATGTAAATATTATTCCCT-3' | This study |
| BG3014 | <i>yopH</i> down R, 5'-GGCGGTGGTACTAAAAATAGG-3' | This study |
| BG3019 | <i>yopJ</i> up F, 5'-TTGCGAGAGCTGACGACCATC-3' | This study |
| BG3020 | <i>yopJ</i> up R + P1, 5'-GAAGCAGCTCCAGCCTACACCATTTATTATCCTTATTCAAGGG-3' | This study |
| BG3021 | <i>yopJ</i> down F + P4, 5'-GGTCGACGGATCCCCGGAATTAAATGTATTGGAAATCTTGCTCC-3' | This study |
| BG3022 | <i>yopJ</i> down R, 5'-CTGGGTATCGGTGCTATGATCG-3' | This study |
| BG3043 | <i>ypkA</i> up F, 5'-CCATCCGATATATCAGTTCCA ACTG-3' | This study |
| BG3044 | <i>ypkA</i> up R + P1, 5'-CCATCCGATATATCAGTTCCA ACTG-3' | This study |
| BG3045 | <i>ypkA</i> down F + P4, 5'-GGTCGACGGATCCCCGGAATCATGCTTACTCATCCCC-3' | This study |
| BG3065 | <i>ypkA-yopJ</i> up F + P1, 5'-GAAGCAGCTCCAGCCTACACCATGCTTACTCATCCCC-3' | This study |

Supplementary References

1. **Doll JM, Zeitz PS, Ettestad P, Bucholtz AL, Davis T, Gage K.** 1994. Cat-transmitted fatal pneumonic plague in a person who traveled from Colorado to Arizona. *Am J Trop Med Hyg* **51**:109–114.
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3. **Price PA, Jin J, Goldman WE.** 2012. Pulmonary infection by *Yersinia pestis* rapidly establishes a permissive environment for microbial proliferation. *Proc Natl Acad Sci U S A* **109**:3083–3088.
4. **Pechous RD, Sivaraman V, Price PA, Stasulli NM, Goldman WE.** 2013. Early Host Cell Targets of *Yersinia pestis* during Primary Pneumonic Plague. *PLoS Pathog* **9**:e1003679.
5. **Palacios M, Broberg CA, Walker KA, Miller VL.** 2017. A Serendipitous Mutation Reveals the Severe Virulence Defect of a *Klebsiella pneumoniae fepB* Mutant. *mSphere* **2**:e00341-17.